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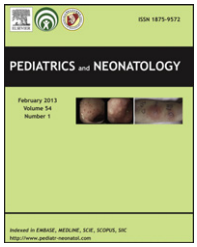

CASE REPORT

Late-Onset Invasive Group B Streptococcal Infection with Serotype VIII in a Neonate Having Congenital Biliary Atresia

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A female newborn was admitted to our department 15 days after birth for insufficient sucking and jaundice. The patient's blood and urine cultures were both positive for group B streptococcal (GBS) infection. A maternal vaginal sample at 35 weeks' gestation was negative for GBS in culture-based microbiologic screening. The patient recovered shortly after receiving systemic antibiotic therapy. On the basis of clinical evidence of white stool and progressive jaundice, we suspected that the newborn had complications related to congenital biliary atresia (CBA); surgery was performed. Isolates from the mother's vaginal sample obtained when the patient was 25 days old, along with neonatal blood, revealed identical patterns (serotype VIII and sequence type 1) of GBS capsular and multilocus sequence typing, suggestive of maternal transmission. Molecular epidemiologic examination may be useful to clarify the transmission route and etiology; culture-based microbiologic screening appears to have limitations for detecting the route of transmission.

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1. Introduction

Group B streptococcus (GBS, *Streptococcus agalactiae*) is a major contributor to invasive infections, such as meningitis and sepsis, in newborns and infants. These infections were classified as early onset (from birth to Day 6) or late onset (from Days 7 to 89). The GBS that causes early-onset infection is usually transmitted from mother to newborn, and late-onset infection is usually transmitted via either horizontal or vertical routes. In Japan, the 2008 obstetric guidelines recommend culture-based microbiologic screening for all pregnant women during weeks 33—37 of gestation.[1] However, because of low screening sensitivity, cases of invasive GBS infection have developed despite negative screening results.[2]

GBS serotypes isolated from children with invasive infections differ from those in adults. In descending order, serotypes III, Ia, and Ib are predominant among children, whereas serotype VIII is a rare type that is detected by polymerase chain reaction (PCR) assay.[3] Multilocus sequence typing is a molecular epidemiologic method used to evaluate the clonality of GBS strains.[4]

We herein report a late-onset serotype VIII GBS infection via vertical transmission with a negative antenatal maternal screening in a neonate having congenital biliary atresia (CBA).

2. Case Report

The affected neonate was a female weighing 2650 g when born at 39 weeks' gestation by vaginal delivery to a 35-year-old primigravida. A maternal vaginal sample obtained at 35 weeks' gestation was negative for GBS according to culture-based microbiologic screening. Neither preterm complications nor prolonged rupture of maternal membranes had occurred. No abnormalities of the placenta or umbilical cord were observed. The Apgar score was 8 at 1 minute and 9 at 5 minutes. At 4 days of age, the newborn received 2 days of phototherapy for idiopathic neonatal jaundice. The infant was discharged at 6 days of age. At 13 days of age, the infant suddenly became unwell, exhibiting insufficient sucking and a pale face. At 15 days of age, the infant remained unwell and the mother brought her daughter to our department. The neonate was hospitalized immediately.

Upon admission, physical examination revealed fever (37.1°C), a pale face with peripheral cyanosis, and irregular respiration with apnea. Her percutaneous saturation of oxygen under room air was unstable (less than 90%), and neither inspiratory crackles nor expiratory rhonchi were apparent upon auscultation. Laboratory findings indicated normal levels of white blood cells (17,400 /μL), platelets (458,000 /μL), and blood glucose (93 mg/dL), as well as elevated concentrations of serum C-reactive protein (2.0 mg/dL), total and direct bilirubin (10.6 mg/dL and 4.17 mg/dL), and γ-GTP (877 IU/L). Examination of the cerebrospinal fluid (CSF) revealed mild increases in cell counts (61/μL) and no decrease in glucose (35 mg/dL). The patient showed no abnormalities in serum immunoglobulins.

GBS was cultured from blood and urine, but not from the CSF or nasopharyngeal specimens. These findings suggested GBS infection and cholestasis. Thus, the patient was treated empirically with combined parenteral antibiotics (ampicillin 120—200 mg/kg/day and ceftriaxone 60 mg/kg/day), along with supportive management, which included an oxygen supplement. The patient's general condition and laboratory results improved rapidly. Following this therapy, the infant was observed to have white-colored stools and progressive jaundice. An abdominal ultrasound revealed no evidence of gallbladder or biliary tract abnormalities. The patient was referred to the department of pediatric surgery in a different specialized hospital, where she was examined for CBA. At 23 days of age, the patient underwent surgery and intrahepatic CBA was diagnosed. Following surgery, and despite 1 month of steroid therapy to prevent cirrhosis of the liver, GBS infection did not recur. At a follow-up assessment 10 months later, the patient exhibited no neurologic sequelae.

When the patient was 25 days of age, written consent was obtained to collect breast milk, a vaginal swab, and an anal swab from the mother to evaluate the route of transmission. These specimens, along with the GBS isolate from the neonatal blood, were sent to the Laboratory of Molecular Epidemiology for Infectious Agents at Kitasato Institute for Life Sciences, Kitasato University, to identify the species and its molecular epidemiology. Real-time PCR, amplifying the GBS-specific *dltS* gene, was used as previously described.[3] Real-time PCR of the vaginal sample revealed *dltS* amplification. GBS was also cultured out of the vaginal sample. However, no pathogens were detected from the anal and breast milk cultures.

We determined the capsular type and multilocus sequence typing for both GBS isolates from the mother's vagina as well as from the child's bloodstream. These examinations indicated that both isolates were identical (serotype VIII and sequence type 1). Additionally, no GBS was identified during routine surveillance for newborns in the neonatal intensive care unit (NICU) using nasopharyngeal swabs, or from standard cultures on samples from children and pregnant women in the same pediatrics and obstetrics ward 1 month before and after this patient's admission.

Table 1 presents microbiologic GBS screening data from pregnant women in our hospital collected during the past 5 years (from April 2006 to March 2011). Of the 1930 cases analyzed at 34—35 weeks' gestation, 72 (3.7%) were positive according to the screening results. Unfortunately, two cases of GBS infection developed following negative screening results. Early-onset GBS sepsis was diagnosed in a patient with progressive respiratory distress, and she manifested no neurologic sequelae after discharge. The other case was the late-onset infection described here.

3. Discussion

The GBS infection described here was late onset and caused by serotype VIII in a neonate with CBA. The primary symptoms of early-onset infections tend to include progressive respiratory distress, whereas symptoms of late-onset infections include insufficient sucking, low activity, and other indicators of unwellness. Sepsis accounts for 44.1% of the cases of late-onset infections, and meningitis

Table 1 Results of antenatal maternal culture-based screening using vaginal swab specimens during the 5-year period (from April 2006 to March 2011).

	Apr 2006 to Mar 2007	Apr 2007 to Mar 2008	Apr 2008 to Mar 2009	Apr 2009 to Mar 2010	Apr 2010 to Mar 2011	Total five years
Negative	395*	412	422	444	185*	1858
Positive	13	10	16	25	8	72
Total	408	422	438	469	193	1930
Positive rate (%)	3.2	2.4	3.7	5.3	4.1	3.7

Seventy-two of 1930 cases (3.7%) had positive results from screening. Asterisks denote two cases of invasive group B streptococcal infection and the negative screening.

accounts for 40.9%.[5] Accordingly, our neonate proceeded through a typical clinical course. Invasive GBS infection caused by serotype VIII was first reported in 1990.[5] In Japan, the most prevalent invasive GBS strain in infants was type III for both early- and late-onset infections. Type VIII strains were detected in 14 of 258 isolates (5.4%) from early- onset disease and in one of 73 isolates (1.4%) from late-onset disease.[6] Type VIII strains were reported to possess some degree of virulence in neonates, producing clinical symptoms (e.g., progressive respiratory distress) similar to those associated with early-onset infection in other common strains.[7] The clinical syndromes presented in this patient were bacteremia and urinary tract infection, similar to those presented in adults with GBS infection and underlying medical conditions. To our knowledge, this is the first report to describe late-onset type VIII GBS infection with congenital abnormality.

Because 95% of these patients presented symptoms within 2 days of birth, early- onset infection is believed to be transmitted by a vertical route. Transmission of late-onset infection seems to occur by both vertical and horizontal routes. Confirmed cases of horizontal transmission have occurred via breast milk.[8] Several reports have also correctly estimated the outbreak of late-onset infections in the same room and department.[9,10] However, no pathogens were detected from a culture of breast milk from this patient's mother. Nor was GBS identified during routine surveillance for newborns in the NICU using nasopharyngeal swabs, or from standard cultures on samples from children and pregnant women in the same pediatrics and obstetrics ward 1 month before or after this patient's admission. These results suggest vertical rather than horizontal transmission. Identical GBS strains, as determined by capsular typing and multilocus sequence typing (sequence type 1), were isolated from the mother's vagina and the child's blood. This finding also supports vertical transmission.

The maternal screening test for GBS was negative for both cases of neonatal GBS infections in the current report. These observations suggest that culture-based microbiologic screening is limited in its capability to detect colonized GBS at delivery. A novel approach is needed to improve sensitivity in order to identify GBS colonization. Vaginal colonization at delivery may differ from colonization during pregnancy because the vaginal pH undergoes significant changes. The PCR assay is a novel method to use instead of the culture.[11] A multiplex real-time PCR assay appears useful for the rapid detection of virulent GBS, and it is a novel antenatal screening method. Clinical trials need to be conducted to assess the efficacy and the costs versus benefits of the PCR assay for future use.

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